Comparison of *Veramyst* with Fexofenadine

This information is provided in response to your request for information about Veramyst® (fluticasone furoate) Nasal Spray.

SUMMARY

- Two well-controlled clinical trials in patients with seasonal allergic rhinitis (SAR) demonstrated that *Veramyst* 110 mcg once-daily provided significantly greater improvements in nighttime symptoms score (NSS), and all other nasal efficacy endpoints (daytime, nighttime, 24-hour, and instantaneous total nasal symptoms scores) compared with fexofenadine and placebo ($P < 0.001$).
- *Veramyst* provided significantly greater improvements in ocular symptoms (daytime, nighttime, 24-hour, and instantaneous total ocular symptoms scores) compared with fexofenadine and placebo ($P \leq 0.034$) in one study. In the other study, improvements in ocular symptoms with *Veramyst* were significantly greater compared with placebo ($P \leq 0.007$) and were comparable with the improvements seen with fexofenadine ($P \geq 0.058$).
- Adverse events reported with *Veramyst* were similar in nature and incidence to those reported in the fexofenadine and placebo groups. The most common adverse events included headache (4%), epistaxis (0-2%), and pharyngolaryngeal pain (1-2%).
- Important safety information is found in the attached Prescribing Information.

COMPARATIVE STUDIES

Two randomized, double-blind, double-dummy, placebo-controlled, parallel-group, 2-week clinical trials evaluated the comparative efficacy and safety of intranasal *Veramyst* and oral fexofenadine in patients ≥12 years with ≥2 year history/diagnosis of seasonal allergic rhinitis (SAR) to mountain cedar (Study 1) or ragweed (Study 2) (positive skin tests).[1,2,3] Prior to randomization, patients were required to have met the following minimum symptom criteria with average scores on any 4 of the last 7 assessments during the 5-21 day pre-treatment screening period: nighttime symptoms score (NSS) ≥4.5, congestion score on awakening assessed for NSS ≥2, daytime reflective total nasal symptoms scores (D-rTNSS) ≥6, reflective nasal congestion score ≥2, daytime reflective total ocular symptoms score (D-rTOSS) ≥4, and diary completion >80%. Randomized patients received either intranasal *Veramyst* 110 mcg and an oral placebo capsule (Study 1: n=312, Study 2: n=224), oral fexofenadine 180 mg and intranasal vehicle-placebo nasal spray (Study 1: n=311, Study 2: n=227), or intranasal vehicle-placebo nasal spray and oral placebo once daily (Study 1: n=313, Study 2: n=229).

The primary efficacy endpoint was the mean change from baseline (MCFB) over the 2-week treatment period in the nighttime symptoms score (NSS) which assessed the impact of nighttime nasal symptoms on sleep using a validated questionnaire. The NSS is obtained from the subject's ratings on awakening each morning, prior to taking their treatment medications, of 3 questions relating to nasal congestion on awakening, nighttime awakenings due to nasal symptoms, and the degree of difficulty going to sleep due to nasal symptoms. Each question is rated utilizing a 0 (none) to 3 (severe) scale.

Secondary efficacy endpoints included MCFB over the 2-week treatment period in reflective total nasal symptoms scores (rTNSS), comprised of nasal itching, sneezing, nasal congestion, and rhinorrhea, and reflective total ocular symptom scores (rTOSS), comprised of eye itching/burning, tearing/watering, and redness, obtained from 12-hour assessments. Terms used for the 12-hour assessment periods represented the period being assessed. Assessments performed in the morning were termed nighttime (N), and

assessments performed in the evening were termed daytime (D). The daytime and nighttime assessments were averaged to derive "24-hour" values which were previously termed "daily" in other fluticasone furoate studies. The names of these assessments were changed in this study to coincide with the primary endpoint, the nighttime symptoms score, which was evaluted in the morning upon awakening. Nasal and ocular symptoms were also rated instantaneously (i) each morning prior to dosing to assess duration of action.

Peak inspiratory nasal flow (PNIF), a measurement of nasal congestion using a hand-held inspiratory flow meter, was also assessed by twice daily patient measurements (in the morning (AM) prior to taking study medication and in the evening (PM)).

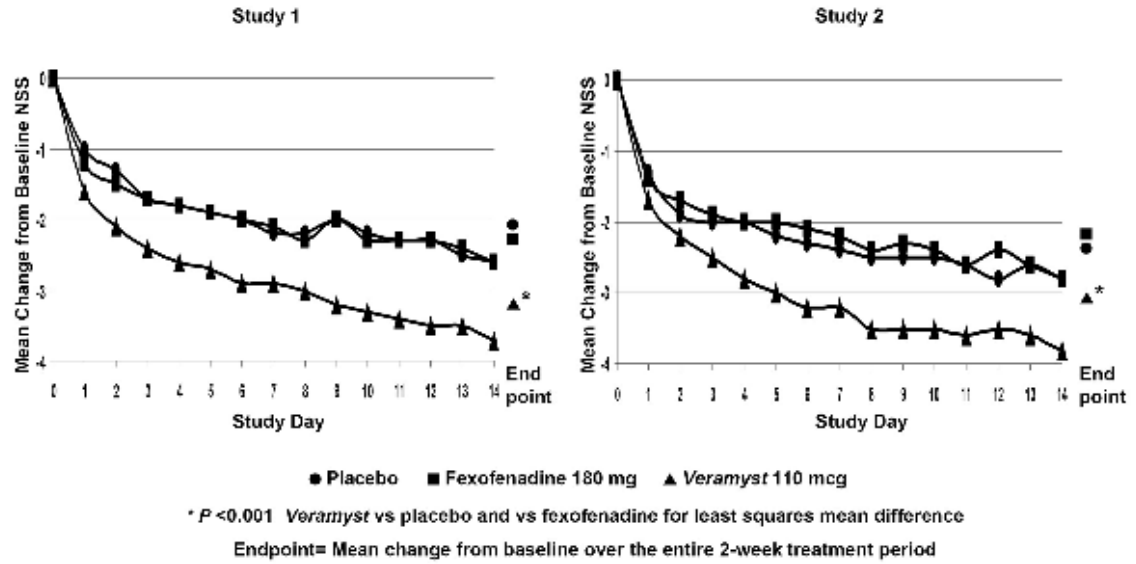
Sleep related quality of life (QOL) was also evaluated by MCFB in the nocturnal rhinoconjunctivitis quality of life questionnaire (NRQLQ) global score. The NRQLQ is a 16-item, self-administered, disease-specific (allergic rhinitis), QOL instrument used to measure the functional problems that are most troublesome to patients with nocturnal allergy symptoms over a 1-week period by assessing four individual NRQLQ domains (sleep problems, sleep time problems, symptoms on waking in morning, practical problems) and an overall global score.

Safety was assessed by adverse events, vital signs, physical examination, and nasal examination.

EFFICACY RESULTS

In both studies, *Veramyst* provided significant improvements in the NSS compared to both fexofenadine and placebo (P <0.001), as illustrated in Figure 1. No difference in the control of nighttime symptoms was seen between fexofenadine and placebo.

Figure 1. Mean Change from Baseline in Nighttime Symptoms Scores (NSS)



In both studies, *Veramyst* also produced significantly greater improvements in all secondary nasal efficacy endpoints (daytime, nighttime, 24-hr, pre-dose TNSS) than fexofenadine or placebo (P <0.001). In Study 2, *Veramyst* provided significantly greater improvements in ocular symptoms (daytime, nighttime, 24-hour, and instantaneous total ocular symptoms scores) compared with fexofenadine and placebo ($P \leq 0.034$). In Study 1, improvements in ocular symptoms with *Veramyst* were significantly greater compared with placebo $P \leq 0.007$) and were comparable with the improvements seen with fexofenadine ($P \geq 0.058$). (Table 1). The PNIF (AM and PM) and NRQLQ (global score) were also significantly improved by *Veramyst* compared with fexofenadine and placebo (P <0.001) in both studies.

Table 1. - See Appendix

Safety

Adverse events reported with *Veramyst* were similar in nature and incidence to those reported in the fexofenadine and placebo groups (Table 2).

Table 2. Adverse Events Occurring ≥1% and More Common than Placebo

Adverse Event	Placebo (Study 1: n=313) (Study 2: n=229)	Fexofenadine (Study 1: n=311) (Study 2: n=227)	*Veramyst* (Study 1: n=312) (Study 2: n=224)
Headache (n,%)	11 (4) 6 (3)	10 (3) 9 (4)	12 (4) 10 (4)
Epistaxis (n,%)	5 (2) 2 (<1)	1 (<1) 4 (2)	7 (2) 0
Pharyngolaryngeal Pain (n,%)	4 (1) 1 (<1)	1 (<1) 3 (1)	5 (2) 3 (1)
Pyrexia (n,%)	2 (<1) 0	4 (1) 0	1 (<1) 0

Some information contained in this response may not be included in the approved Prescribing Information for this product. The comparator data cited in this response does not necessarily establish superior or comparable safety or efficacy. This response is not intended to offer recommendations for administering our product in a manner inconsistent with its approved labeling.

In order for GlaxoSmithKline to monitor the safety of our products, we encourage healthcare professionals to report adverse events or suspected overdoses to the company at 888-825-5249. Please consult the attached Prescribing Information.

This response was developed according to the principles of evidence-based medicine and, therefore, references may not be all-inclusive.

Enclosure: Prescribing Information for *Veramyst*

REFERENCE(S)

1. Andrews C, Martin B, Jacobs R, et al. Efficacy of Fluticasone Furoate Nasal Spray versus Oral Fexofenadine on Nighttime Sleep Disturbance Caused by Seasonal Allergic Rhinitis (SAR) Nasal Symptoms. American College of Asthma, Allergy and Immunology 2007 Annual Scientific Meeting, Gaylord Texan Resort & Convention Center, Grapevine, TX. November 8-14, 2007. Abstract 13. (oral presentation) (Study FFU109045) *
2. Data on File. Study FFU109045 (RM2007/0031/00). *
3. Data on File. Study FFU109047 (RM2007/00866/00). *

Appendix

Table 1. Change from Baseline in Primary and Secondary Endpoints

Endpoint*	Mean Change			LS Mean Difference (95% CI)			*P*-value		
Study 1 Study 2	Placebo (n=313) (n=229)	FEX (n=311) (n=227)	FFNS (n=312) (n=224)	FEX vs Placebo	FFNS vs Placebo	FFNS vs FEX	FEX vs Placebo	FFNS vs Placebo	FFNS vs FEX
NSS†									
	-1.9	-2.0	-2.9	0.0 (-0.3,0.2)	-1.0 (-1.2,-0.7)	-0.9 (-1.2,-0.7)	0.816	<0.001	<0.001
	-2.3	-2.2	-3.1	0.1 -0.2,0.5	-0.8 -1.1,-0.4	-0.9 -1.2,-0.6	0.374	<0.001	<0.001
N-rTNSS‡									
	-2.5	-2.7	-3.7	-0.3 (-0.6,0.1)	-1.3 (-1.6,-0.9)	-1.0 (-1.4,-0.7)	0.136	<0.001	<0.001
	-2.9	-2.9	-4.1	0.1 -0.3,0.5	-1.2 -1.6,-0.8	-1.3 -1.7,-0.9	0.632	<0.001	<0.001
D-rTNSS‡									
	-2.6	-3.0	-3.7	-0.3 (-0.7,0.1)	-1.1 (-1.5,-0.7)	-0.8 (-1.2,-0.4)	0.136	<0.001	<0.001
	-3.0	-2.9	-4.2	0.2 -0.2,0.6	-1.2 -1.6,-0.7	-1.4 -1.8,-0.9	0.632	<0.001	<0.001
24hr-rTNSS‡									

* entire treatment period; † primary efficacy endpoint; ‡ key secondary endpoint; § other secondary endpoint

KEY: LS=Least Square; CI=Confidence Interval; FEX=fexofenadine; FFNS=fluticasone furoate nasal spray; NSS=nighttime symptoms score; TNSS=total nasal symptoms score; r=reflective; i=instantaneous; N=nighttime; D=daytime; TOSS=total ocular symptoms score; AM=morning; PM=evening; PNIF=peak nasal inspiratory flow; NRQLQ=nocturnal rhinoconjuntivitis quality of life questionnaire

Endpoint*	Mean Change			LS Mean Difference (95% CI)			*P*-value		
	Placebo (n=313) (n=229)	FEX (n=311) (n=227)	FFNS (n=312) (n=224)	FEX vs Placebo	FFNS vs Placebo	FFNS vs FEX	FEX vs Placebo	FFNS vs Placebo	FFNS vs FEX
Study 1	-2.5	-2.8	-3.6	-0.3 (-0.6,0.1)	-1.2 (-1.6,-0.8)	-0.9 (-1.3,-0.6)	0.136	<0.001	<0.001
Study 2	-2.8	-2.8	-4.1	0.2 -0.3,0.6	-1.2 -1.6,-0.8	-1.3 -1.7,-0.9	0.632	<0.001	<0.001
Pre-dose iTNSS‡									
	-2.3	-2.6	-3.6	-0.2 (-0.6,0.1)	-1.3 (-1.7,-1.0)	-1.1 (-1.4,-0.7)	0.193	<0.001	<0.001
	-2.8	-2.7	-4.1	0.2 -0.2,0.6	-1.3 -1.7,-0.8	-1.5 -1.9,-1.1	0.484	<0.001	<0.001
N-rTOSS‡									
	-2.0	-2.2	-2.5	-0.2 (-0.5,0.1)	-0.5 (-0.8,-0.2)	-0.3 (-0.6,0.0)	0.286	0.001	0.106
	-2.3	-2.2	-2.7	0.1 -0.2,0.5	-0.4 -0.8,-0.1	-0.6 -0.9,-0.2	0.400	0.034	0.002
D-rTOSS‡									
	-2.2	-2.4	-2.6	-0.2 (-0.5,0.1)	-0.4 (-0.7,-0.1)	-0.2 (-0.5,0.1)	0.286	0.007	0.106
	-2.5	-2.4	-2.9	0.2 -0.1,0.6	-0.4 -0.7,-0.0	-0.6 -0.9,-0.2	0.400	0.034	0.002
24hr-rTOSS‡									

* entire treatment period; † primary efficacy endpoint; ‡ key secondary endpoint; § other secondary endpoint
KEY: LS=Least Square; CI=Confidence Interval; FEX=fexofenadine; FFNS=fluticasone furoate nasal spray; NSS=nighttime symptoms score; TNSS=total nasal symptoms score; r=reflective; i=instantaneous; N=nighttime; D=daytime; TOSS=total ocular symptoms score; AM=morning; PM=evening; PNIF=peak nasal inspiratory flow; NRQLQ=nocturnal rhinoconjuntivitis quality of life questionnaire

Endpoint*	Mean Change			LS Mean Difference (95% CI)			*P*-value		
	Placebo (n=313) (n=229)	FEX (n=311) (n=227)	FFNS (n=312) (n=224)	FEX vs Placebo	FFNS vs Placebo	FFNS vs FEX	FEX vs Placebo	FFNS vs Placebo	FFNS vs FEX
Study 1	-2.0	-2.2	-2.5	-0.2 (-0.5,0.1)	-0.5 (-0.7,-0.2)	-0.3 (-0.6,0.0)	0.286	0.003	0.106
Study 2	-2.3	-2.2	-2.7	0.2 -0.2,0.5	-0.4 -0.7,-0.1	-0.5 -0.9,-0.2	0.400	0.034	0.002
Pre-dose iTOSS‡									
	-1.9	-2.2	-2.4	-0.3 (-0.5,0.0)	-0.5 (-0.8,-0.2)	-0.3 (-0.6,0.0)	0.160	<0.001	0.058
	-2.2	-2.2	-2.7	0.1 -0.2,0.5	-0.4 -0.8,-0.1	-0.6 -0.9,-0.2	0.484	0.014	0.002
AM PNIF§									
	1.7	1.4	9.9	-0.4 (-3.6,2.7)	8.4 (5.3,11.5)	8.8 (5.7,11.9)	0.779	<0.001	<0.001
	4.8	2.2	13	-2.6 -6.4,1.2	8 4.2,11.8	10.6 6.8,14.4	0.176	<0.001	<0.001
PM PNIF§									
	0.2	1.3	7.1	0.7 (-2.5,4.0)	7.0 (3.8,10.3)	6.3 (3.1,9.6)	0.662	<0.001	<0.001
	2.3	0.3	9.7	-2.0 -6.1,2.1	7.3 3.2,11.5	9.3 5.2,13.4	0.350	<0.001	<0.001

* entire treatment period; † primary efficacy endpoint; ‡ key secondary endpoint; § other secondary endpoint
KEY: LS=Least Square; CI=Confidence Interval; FEX=fexofenadine; FFNS=fluticasone furoate nasal spray; NSS=nighttime symptoms score; TNSS=total nasal symptoms score; r=reflective; i=instantaneous; N=nighttime; D=daytime; TOSS=total ocular symptoms score; AM=morning; PM=evening; PNIF=peak nasal inspiratory flow; NRQLQ=nocturnal rhinoconjuntivitis quality of life questionnaire

Endpoint*	Mean Change			LS Mean Difference (95% CI)			*P*-value		
Study 1 Study 2	Placebo (n=313) (n=229)	FEX (n=311) (n=227)	FFNS (n=312) (n=224)	FEX vs Placebo	FFNS vs Placebo	FFNS vs FEX	FEX vs Placebo	FFNS vs Placebo	FFNS vs FEX
NRQLQ§									
	-1.3	-1.5	-1.9	-0.1 (-0.4,0.1)	-0.6 (-0.8,-0.4)	-0.5 (-0.7,-0.3)	0.203	<0.001	<0.001
	-1.4	-1.4	-2.0	0.0 -0.2,0.3	-0.6 -0.9,-0.4	-0.7 -0.9,-0.4	0.791	<0.001	<0.001

* entire treatment period; † primary efficacy endpoint; ‡ key secondary endpoint; § other secondary endpoint
KEY: LS=Least Square; CI=Confidence Interval; FEX=fexofenadine; FFNS=fluticasone furoate nasal spray; NSS=nighttime symptoms score; TNSS=total nasal symptoms score; r=reflective; i=instantaneous; N=nighttime; D=daytime; TOSS=total ocular symptoms score; AM=morning; PM=evening; PNIF=peak nasal inspiratory flow; NRQLQ=nocturnal rhinoconjuntivitis quality of life questionnaire